REMARKS

It is respectfully requested that this application be reconsidered in view of the above amendments and the following remarks.

Amendments

Claims 1-10 have been canceled without prejudice or disclaimer in view of the restriction and election of species requirement issued for this application (Paper No. 18). Applicants reserve the right to file one or more divisional applications directed to the canceled subject matter.

Claims 24 has been amended to recite that the inflammatory condition is mediated at least in part by the $\alpha_9\beta_1$ integrin. Support for this amendment is found, in Applicants' specification at, for example, page 3, lines 23, et seq. Claim 24 has been still further amended to make this claim more readable and to specifically reference the assay in the selecting process.

As required by 37 C.F.R. §1.121, the changes to the claims arising from these amendments are specified in the attached Appendix. In addition, a conformed copy of the pending applications is attached.

Entry of these amendments is earnestly solicted.

Restriction Requirement

In the Office Action, a restriction requirement was set forth in two parts. Specifically, subgenera were defined therein as follows:

G1: within this subgenus, both the following conditions are met:

a) the assay system requires the presence of both an alpha-9 integrin and an alpha-9 integrin ligand; and

b) the "activity" referred to in Claim 24 is that of the propensity of the recited compounds to compete with an alpha-9 integrin ligand for binding to the alpha-9 integrin.

G2: in this subgenera, at least one of the following conditions is met:

a) the assay system does not require the presence of an alpha-9 integrin;

b) the assay system does not require the presence of an alpha-9 integrin ligand; and

c) the "activity" referred to in Claim 24 can be anything that can be measured in a biological assay, as long as it does not require binding to alpha-9 integrin.

G3: the compound that is administered to the subject (Claim 31) is limited to those recited in Claims 34-36.

G4: the compound used in the method of Claim 31 can be whatever is permitted by the claims, provided that G3 is excluded.

With the subgenera described above, the Examiner has restricted the claims in this application under 35 U.S.C. §121 into the following Groups:

1. Claims 1-10, drawn to compositions which contain alpha-9 integrin antagonists

2. Claims 24-27, 29, 30, drawn to a method of conducting an assay which is limited to G1, and which measures binding between alpha-9 integrin and a cognate ligand.

3. Claims 24-27, 29, 30, drawn to a method of conducting an assay which is limited to G2, and which measures binding between alpha-9 integrin and a cognate ligand.

4. Claim 28, drawn to a method of measuring competition between VCAM-1 and a test compound for binding to an alpha-4/beta-1 integrin.

5. Claims 31-36, drawn to a method of treating an inflammatory condition, limited to G3.

6. Claims 31-36, drawn to a method of treating an inflammatory condition, limited to G4.

This restriction requirement is traversed-in-part for the following reasons.

Applicants maintain that G1 and G2 should be combined because Claim 24, as now presented, unambiguously recites that the compound exhibit a binding inhibitory activity in the assay system which measures the amount of alpha-9 integrin binding. In the Office Action, subgenera G1 was referenced relative to an α-9 integrin assay whereas subgenera G2 was referenced as not requiring the α-9 integrin. However, as now presented, Claim 24 specifically sets forth a method for screening compounds effective in treating inflammation mediated at least in part by the $\alpha_9\beta_1$ integrin. The issue raised at pages 3 and 4 of the Office Action, which necessitated bisecting these embodiments, has been obviated. Recombination of these groups is requested.

As to Claim 28, Applicants disagree with the analysis that this claim is not properly subgeneric to any of the preceding claims.[1] As noted in the specification (e.g., page 7, lines 7-21), preferred test compounds for inclusion in this method include those which exhibit activity in modulating, particularly inhibiting, binding between the $\alpha_4\beta_1$ integrin and any of its ligands. That is to say, that the compounds useful in this invention in binding to the $\alpha_9\beta_1$ integrin are preferably chosen from those already exhibiting activity, as above, between the $\alpha_4\beta_1$ integrin and any of its ligands. As such, the recitation in Claim 28 does not define an assay protocol not requiring the α-9 integrin. Rather, this claim is merely stating how to determine what compounds exhibit activity between the $\alpha_4\beta_1$ integrin and any of its ligands so these compounds can be used in the α-9 integrin assay.

[1] See, for example, the paragraph bridging pages 4 and 5 of the Office Action.

Applicants further maintain that subgenera G3 and G4 should be combined. Subgenera G4 is generic to subgenera G3. Specifically, subgenera G4 includes generic Claim 31 to the extent that this claim encompasses species in addition to those recited in Claims 34-36 which are encompassed in subgenera G3. Moreover, Claims 34-36 recite a reasonable number of species related to the genus of Claim 31. Such is clearly permitted and should not be restricted. See, for example, MPEP §806(A). In view of the above, Applicants submit that subgenera G3 and G4 should be combined.

Based on the above, Applicants request that this restriction requirement be recast as follows:

Subgenera G1′: Assay Systems of Claims 24-30; and

Subgenera G2′: Method of treatment Claims 31-36.

If the subgenera were so recast, the specific groups arising from restriction would be as follows:

1. Claims 1-10, drawn to compositions which contain alpha-9 integrin antagonists

2. Claims 24-30, drawn to a method of conducting an assay

3. Claims 31-36, drawn to a method of treating an inflammatory condition

Election

Notwithstanding the above traversal, Applicants are required to make an election consistent with the restriction requirement found in the Office Action (Paper No. 18). Accordingly, Applicants elect, with traverse (as noted above), Group 5 (i.e., a method of treating an inflammatory condition, limited to G3).

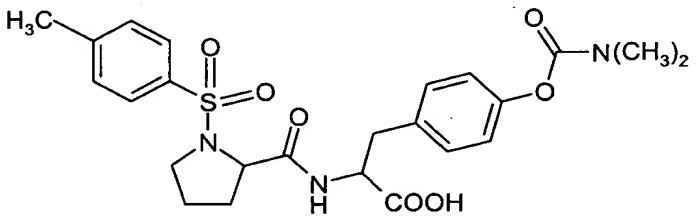
Election of Species

In the event that Applicants elected Group 5 or 6, the Office Action further required Applicants to make a species election from the following:

a) a specific α-9 antagonist compound that is administered to the subject; and

b) a specific "inflammatory condition".

With regard to the above, Applicants elect, without traverse, as their specific α-9 antagonist compound, N-(toluene-4-sulfonyl)-L-prolyl-L-4(N,N-dimethylcarbamyl-oxy)phenylalanine, which is represented by the formula:



The elected compound is the second compound recited in Claim 34.

In addition, Applicants elect, again without traverse, as their specific inflammatory condition "asthma" which is recited in the specification at, for example, 4, lines 1-7.

Applicants believe that Claims 31-33 and 35-36 read on these elected species.

Early examination on the merits is earnestly solicited.

Respectfully submitted,

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Attachment to Reply and Amendment dated April 11, 2002
Marked-up Copy

Claim 24 has been amended as follows:

24. (amended) A method of screening for therapeutic compounds effective in treating an inflammatory condition mediated at least in part by the $\alpha_9\beta_1$ integrin, which method comprises: [comprising]

adding a test compound to an assay system which measures an amount of alpha-9 integrin binding to an alpha-9 integrin ligand, and

selecting the test compound as an effective therapeutic drug candidate, if said compound exhibits, in said assay, a binding inhibitory activity that is at least 1/1000 as potent as an activity exhibited by a compound selected from the group consisting of:

N-(toluene-4-sulfonyl)-L-prolyl-L-4(4-methylpiperzin-1-ylcarbonyloxy)phenyl-alanine,

N-(toluene-4-sulfonyl)-L-prolyl-L-4(N,N-dimethylcarbamyloxy)phenylalanine,

N-(1-methylpyrazole-4-sulfonyl)-L-prolyl-L-4-(N,N-dimethylcarbamyloxy)phenyl-alanine,

N-(toluene-4-sulfonyl-)-L-(1,1-dioxo-5,5-dimethyl)thiaprolyl-L-4-(N,N-dimethyl-carbamyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-N-methyl-L-alaninyl-L-4-(N,N-dimethylcarbamyloxy)phenyl-alanine,

N-(toluene-4-sulfonyl)-L-[1,1-dioxo)thiamorpholin-3-carbonyl]-L-4-(N,N-dimethyl-carbamyloxy)phenylalanine,

N-(N-*p*-toluenesulfonyl)prolyl-4-(piperazinoyloxy)phenylalanine,

N-(N-*p*-toluenesulfonyl)sarcosyl-4-(N,N-dimethylcarbamyloxy)phenylalanine, and

N-(toluene-4-sulfonyl)-L-(5,5-dimethyl)thiaprolyl-L-4-[3-(N,N-dimethyl)-propoxy]phenylalanine.